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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,688	ORSON ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *5,16 and 43-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-15 and 17-42* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☒ Claim(s) *5,16 and 43-57* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3 and 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-57 are pending in the present application.

Applicant's election without traverse of the invention of Group I (claims 1-42) in Paper No. 5 is acknowledged. Applicants further elected without traverse genes associated with an infectious disease and HIV as a pathogenic viral genome, as elected species.

Claims 43-57 are withdrawn from further consideration because they are drawn to non-elected inventions. Additionally, claims 5 and 16 are also withdrawn from further consideration because they are drawn to non-elected species.

Accordingly, claims 1-4, 6-15 and 17-42 are examined on the merits herein.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See page 16, line 9. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-15 and 17-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

(a) A method of producing a composition comprising the step of incubating an expression vector with an aggregated protein-polycationic polymer conjugate to form DNA particles wherein the expression vector comprises a promoter polynulcleotide sequence operatively linked to a polynucleotide sequence encoding an antigen;

(b) A method of inducing an immune response in a mammal comprising the step of administering to the mammal an expression vector bound to an aggregated protein-polycationic polymer conjugate wherein the expression vector comprises a promoter polynucleotide sequence operatively linked to a polynucleotide sequence encoding an antigen;

(c) A method of inducing an immune response in a mammal comprising the step of co-administering to the mammal an expression vector bound to an aggregated protein-polycationic polymer conjugate wherein the expression vector comprises a promoter polynucletoide sequence operatively linked to a polynucleotide sequence encoding an antigen and a cytokine expression vector; wherein said cytokine expression vector is bound to said aggregated protein-polycationic polymer conjugate;

(d) A method of inducing an immune response in a mammal comprising the step of administering to the mammal an expression vector bound to an aggregated protein-polycationic polymer conjugate wherein the expression vector comprises a first promoter polynucleotide sequence operatively linked to a first polynucleotide sequence encoding an antigen and a second polynucleotide sequence encoding a cytokine;

does not reasonably provide enablement for a method of producing a DNA vaccine or a method of treating a condition in an organism using a DNA vaccine or methods of inducing an immune response in an organism as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

Claims 12-15 and 17-27 are drawn to a method of producing a DNA vaccine comprising the step of incubating an expression vector with an aggregated protein-polycationic polymer conjugate to form DNA particles wherein the expression vector comprises a promoter polynulcleotide sequence operatively linked to a polynucleotide sequence encoding an antigen, and a method of treating a condition in an organism by administering to the organism the same DNA vaccine. Claims 28-41 are drawn to methods of inducing an immune response in an organism using an expression vector bound to an aggregated protein-polycationic polymer conjugate of the presently claimed invention.

The instant specification is not enabled for the present broadly claimed invention for the following reasons. With respect to claims 12-15 and 17-23, the instant specification fails to provide sufficient guidance for a skilled artisan on how to use a DNA vaccine of the presently claimed invention for obtaining any prophylactic and/or therapeutic effects and for treating any condition encompassing a host of infectious diseases caused by pathogenic virus, bacterium, fungus and protozoa, cancer and autoimmune diseases in any organism using the same DNA vaccine. Although the exemplification showing that upon intravenous, oral and intradermal administration of an expression plasmid vector bound to a macroaggregated albumin (MAA)-polyethyleneimine (PEI) conjugate into a mammal (mice and macaques) both systemic and mucosal immune responses were elicited, however it is unclear whether these induced immune responses are sufficient to prevent or eradicate or treat a host of infectious diseases, cancers and autoimmune diseases. The nature of the instant claims falls within the realm of the genetic vaccination art that at the effective filing date of the present application remains unpredictable with respect to obtaining prophylactic and therapeutic effects. Chattergoon et al. (FASEB J. 11:753-763, 1997) state "Though DNA vaccines have shown promise in animal models and have raised hopes, the technology is considered an emerging technology" (column 1, paragraph 2, page 762). More recently, Leitner et al. (Vaccine 18:765-777, 2000) state "Although genetic vaccines have been significantly improved, they may not be sufficiently immunogenic for therapeutic vaccination of patients with infectious disease or cancer in clinical trials" (Abstract, page 765). Leitner et al. also listed several variable factors affecting the

immunogenicity of genetic vaccines. These include: the structure of the plasmid backbone, amount of plasmid delivered, expression levels of the antigen, age and strain of the particular species, target tissue, and route of immunization among others (See Table 1, page 767). Additionally with respect to the elected species of a HIV viral genome, the sole purpose for a method of treating and a DNA vaccine containing HIV viral genome is for attaining prophylactic and therapeutic effects in humans due to the specific infection of HIV in a human host. The instant specification is not enabled for such an embodiment for the reasons already discussed above. Additionally, McCluskie et al. (Mol. Med. 5:287-300, 1999) state "[I]t is probably safe to say that any vaccine that works in a human will work in a mouse, but not necessarily vice versa. Therefore, it is difficult to predict from mouse studies the potential of a new vaccine for humans. In fact, in those human trials that have carried out, none of the DNA vaccines induced the strong immune responses that had been seen in mice with the same vectors" (col. 2, last paragraph, page 296). There is no correlation between the observed induced immune responses in mice and macaques reported in the present application with any prophylactic and therapeutic effects achieving in humans against HIV infection, an effective DNA vaccine for which still remains elusive. The instant specification fails to provide sufficient guidance, particularly in the absence of any relevant *in vivo* example (part of guidance), for a skilled artisan on how to achieve any prophylactic and/or therapeutic effects in treating any conditions, particularly for HIV infection, in any organism using the DNA vaccine of the presently claimed invention. As such, it would

have required undue experimentation for a skilled artisan to use the DNA vaccine and to practice a treatment method as claimed.

Moreover, the physiological art is recognized as unpredictable (MPEP 2164.03). As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

With respect to the breadth of the instant claims encompassing treating or preventing any infectious disease caused by any virus, bacterium, fungus, protozoa; any cancer and any autoimmune disease, Applicant is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In the absence of sufficient guidance provided by the specification, it would have required undue experimentation for a skilled artisan to make and use the the instant broadly claimed invention.

With respect to the breadth of the instant claims encompassing treating or inducing an immune response in any organism including humans, cows, horses, dogs, cats, birds, chickens, fishes, frogs, reptiles or any organism having at least on organ,

the instant specification is not enabled for such a broadly claimed invention. Apart from the exemplifications using mice and macaques, it is unclear whether the composition of the presently claimed invention is capable of inducing an immune response that has a substantial and beneficial use in the numerous species encompassed within the broad genus of an organism in the methods as claimed. It is unclear whether the immune components of a fish or a frog or any organism having at least one organ would react to an antigen in a similar manner as those of a mammal to induce an immune response having a beneficial use. An extensive search for the prior art at the effective filing date of the present application revealed that little has been known about the immune responses in species such as frog, fish or chicken, let alone for any organism as contemplated by Applicants. As such, with the lack of sufficient guidance provided by the instant specification, it would have required undue experimentation for a skilled artisan to make and use the methods as claimed. Again, it should be noted that the physiological art is recognized as unpredictable (MPEP 2164.03). Additionally, the courts have also stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application (27 USPQ2d 1662 *Ex parte Maizel.*).

With respect to claims 32-38, as written the cytokine expression vector is not required to be bound to an aggregated protein-polycationic polymer conjugate. The instant specification is not enabled for this embodiment because it fails to provide sufficient guidance for a skilled artisan on how to deliver the cytokine expression vector to the same site as that of an expression vector coding for an antigen that is bound to

an aggregated protein-polycationic polymer conjugate to influence the local cytokine environment and an immune response to said antigen to yield beneficial uses, particularly via any route of administration. Vector targeting *in vivo* to desired cells or tissues continues to be unpredictable and inefficient. This is supported by numerous teachings in the art. For example, Miller & Vile (FASEB 9:190-199, 1995) reviewed the types of vectors available for *in vivo* gene therapy, and concluded that ""for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances ... Targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain (Exp. Opin. Ther. Patents 8:53-69, 1998) reviewed new gene delivery techniques under experimentation that show promises. One of which is the ligand-targeted receptor-mediated vector approach with a relatively higher level of tissue specificity than viruses can offer. However, this approach to gene therapy is much less efficient than viral gene delivery (col. 1, last paragraph, page 65). Verma & Somia (Nature 389:239-242,1997) reviewed various vectors known in the art for use in gene therapy, and the problems that are associated with each. They also indicated clearly that resolution to vector targeting had not been achieved in the art (see the entire article). Verma & Somia also discussed the role of the immune system in inhibiting an efficient targeting of viral vectors to desired targeted cells or tissues (see page 239, and second and third columns of page 242). Verma & Somia also indicated that appropriate enhancer-promoter sequences can improve expression, but that the "search for such combinations is a case of trial and

error for a given cell type." (page 240, sentence bridging columns 2 and 3). The instant specification fails to teach one of skilled in the art how to overcome the unpredictability for vector targeting *in vivo* such that an efficient transfer and expression of a cytokine at the same site where the antigen is expressed so that a beneficial induction of an immune response specific for the antigen could be obtained. Furthermore, as written the naked cytokine expression vector would be subjected to a rapid degradation, particular through a systemic delivery, prior to its entry into cells for expression to yield any beneficial use. With the lack of sufficient guidance provided by the instant specification, it would have required undue experimentation for a skilled artisan to make and use the full scope of the method as claimed.

Accordingly, due to the lack of sufficient direction or guidance provided by the specification regarding to the issues set forth above, the unpredictability of the physiological and genetic vaccine arts, and the breadth of the claims, it would have required undue experimentation to make and use the instant broadly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7-8 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Kircheis et al. (Gene therapy 4:409-418, 1997; IDS).

Claims 1 and 7-8 are drawn to a composition comprising an expression vector bound to an aggregated protein-polycationic polymer conjugate, wherein the expression vector comprises a promoter polynucleotide sequence operatively linked to a polynucleotide sequence encoding an antigen; the same wherein the polycationic polymer is selected from the group consisting of polymamino acids, polyimines or a combination thereof, and preferably the polyimine is polyetheyleneimine. Claim 42 is drawn to a method of introducing genes into a cell comprising the steps of: forming a DNA particle comprising an expression vector bound to an aggregated protein-polycationic polymer conjugate, wherein the expression vector comprises a promoter polynucleotide sequence operatively linked to a polynucleotide sequence encoding an antigen; and incubating the cells with the DNA particle under conditions wherein the cells take in the DNA particle.

Kircheis et al. disclose the preparation of DNA complexes of ligand-polyethylenimine (PEI) conjugates for transfection of cultured neuroblastoma Neuro 2A cells, melanoma B16 or H225 cells, erythroid leukemic K562 cells and T cell leukemia Jurkat E6.1 cells, wherein the ligand is transferrin or CD3 antibody (see abstract). During the synthesis of transferrin-PEI or antiCD3-PEI conjugates, transferrin and antiCD3 molecules would be linked together in addition to them being linked to PEI molecules (see pages 416-417 for their synthesis procedures). As transferrin and antiCD3 molecules are proteins and they are bound together via the modification (qualified as an aggregate according to the definition in the instant specification on page 8, second last paragraph). Furthermore, the transferring-PEI and antiCD3-PEI

complexes are aggregates. The DNA utilized in the study of Kircheis et al. include a plasmid pCMVL coding for the *Photinus pyralis* lucifease gene, the plasmid pCMVβ coding for galatosidase, the plasmid pWS2m coding for murine IL-2, all of which under the control of the cytomegalovirus enhancer/promoter (page 416, col. 2, under the section titled "Cells and vectors"). Galacosidase, lucififerase and murine IL-2 are capable of provoking an immune response in certain hosts, and thereby they are antigens. Kircheis et al. further teach that ligand-conjugated polyethylenimines mediate efficient and enhanced transfection of cultured tumor cells (see Figs. 1-4), and these may be promising vectors for receptor-specific gene delivery (page 409, col. 2, last sentence).

Accordingly, Kircheis et al. anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 7-11, 28-30 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnston et al. (U.S. Patent No. 5,703,057) in view of Kircheis et al. (Gene therapy 4:409-418, 1997; IDS).

Johnston et al. disclose a composition comprising expression vectors encoding antigens prepared from gene sequences derived from a pathogenic virus, including HIV, for expression in a mammalian cell and a method for generating an immune response into a mammal using the same via various modes of administration including parenteral as well as mucosal routes (see Summary of Invention, cols. 2-8; col. 11). Johnston et al. further teach that mammalian genes fused to the pathogen DNA can facilitate expression in the mammalian cell, specifically human growth hormone, ubiquitin, signal sequences and others (col. 5, lines 19-29). Johnston et al. disclose that fusion of nonmammalian pathogen sequences to mammalian genes increases the amount of antigen available to the immune system due to increasing antigenic recognition or targeting to components in the cell. Johnston et al. do not teach that the expression vectors encoding antigens prepared from gene sequences derived from a pathogenic virus, including HIV, for expression in a mammalian cell are bound to an aggregated protein-polycationic polymer conjugates.

However, at the effective filing date of the present application Kircheis et al. disclose the preparation of DNA complexes of ligand-polyethylenimine (PEI) conjugates

for transfection of various cultured tumor cells, wherein the ligand is transferrin or CD3 antibody (see abstract). During the synthesis of transferrin-PEI or antiCD3-PEI conjugates, transferrin and antiCD3 molecules would be linked together in addition to them being linked to PEI molecules (see pages 416-417 for their synthesis procedures). As transferrin and antiCD3 molecules are proteins and they are bound together via the modification (qualified as an aggregate according to the definition in the instant specification on page 8, second last paragraph). Furthermore, the transferring-PEI and antiCD3-PEI complexes are aggregates. Kircheis et al. note that ligand-conjugated polyethylenimines mediate efficient and enhanced transfection of cultured tumor cells (see Figs. 1-4), and these may be promising vectors for receptor-specific gene delivery (page 409, col. 2, last sentence).

Accordingly, at the time of the instant invention it would have been obvious and within the scope of skill for an ordinary skilled artisan to modify the method of Johnston et al. by preparing the composition comprising expression vectors encoding antigens prepared from gene sequences derived from a pathogenic virus, including HIV, bound to a ligand-PEI conjugates for antigen expression in a mammalian cell, particularly immune effector cells, at a target tissue or site to induce an immune response in a mammal based on the teachings of Kircheis et al.

An ordinary skilled artisan would have been motivated to make this modification because as taught by Kircheis et al., ligand-conjugated polyethylenimines mediate an efficient and enhanced transfection, and that these are promising vectors for receptor-specific gene delivery. An enhanced cell transfection rate would be advantageous for

induction of a host immune response specific to an antigen due an increased in the amount of antigen available to the host immune system.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 32-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnston et al. (U.S. Patent No. 5,703,057) in view of Kircheis et al. (Gene therapy 4:409-418, 1997; IDS) and Weiner et al. (U.S. 6,348,449).

The teachings of Johnston et al. and Kircheis et al. have been discussed above. However, none of the references teaches a method for inducing an immune response in a mammal by coadministering into the mammal an expression vector coding for an antigen bound to an aggregated protein-polycationic polymer conjugate and a cytokine expression, or the a method of inducing an immune response in a mammal by administering an expression vector coding an antigen and a cytokine bound to an aggregated protein-polycationic polymer conjugate.

However, at the effective filing date of the present application, Weiner et al. already teach that for immunization applications, the genetic construct contains nucleotide sequences that encode a target protein and further include genes for proteins which enhance the immune response against such target protein. Examples of such genes are those which encode cytokines and lymphokines such as GM-CSF, IL-2, PDGF, IL-1, and others (line 60 of col. 5 continues to line 4 of col. 6, and see the claims).

Accordingly, at the time of the instant invention it would have been obvious and within the scope of skill for an ordinary skilled artisan to further modify the method of Johnston et al. and Kircheis et al. by further incorporating a cytokine expression vector bound to the same aggregated protein-polycationic polymer conjugate or using an expression vector encoding both an antigen and a cytokine that is bound in an aggregated protein-polycationic polymer conjugate. It would have been obvious and within the scope of skill for an ordinary skilled artisan to use the same or different promoters for expressing the sequences encoding an antigen and a cytokine as long as the antigen and cytokine are expressed.

An ordinary skilled artisan would have been motivated to make the above modification because as taught by Weiner et al., the co-expression of cytokines and lymphokines such as GM-CSF, IL-2 and others can enhance the immune response against the desired target protein, for this instance an HIV antigen.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusions

Claim 6 is objected because it is dependent on the rejected claim 1.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's mentor, Dave Nguyen, may be reached at (703) 305-2024, or SPE, Irem Yucel, Ph.D., at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636.

Quang Nguyen, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER